REMARKS

Claims 1, 4, 6, 8, 10, 12, 13 and 21-24 are under examination and currently stand rejected. Claims 2, 3 and 14-20 were cancelled prior to this response. Claims 5, 7, 9, 11 and 25 are withdrawn.

Applicants have amended claim 1, and cancelled claims 21-25 without prejudice or disclaimer. Applicants request entry of the amendment and reserve the right to pursue the cancelled subject matter in another application.

AMENDMENTS TO THE SPECIFICATION

Applicants request that the following amendments be made to the Specification. The changes are made to reflect the use of trademarks and to comply with USPTO practice for citing trademarked products. No new matter is introduced in these amendments.

AMENDMENTS TO THE CLAIMS

Applicants have amended claim 1 to replace "chronic airway remodeling" with "subepithelial fibrosis and matrix deposition." The amendment finds support for example at paragraph [0002], which describes chronic airway remodeling as including subepithelial fibrosis and matrix deposition, and therefore does not present new matter.

CLAIM REJECTIONS – 35 USC § 103

Claims 1, 4, 6, 12, 13 and 21-24

Claims 1, 4, 6, 12, 13 and 21-24 stand rejected under 35 USC 103(a) for allegedly being unpatentable over Ochoa *et al.,* (US 2004/0057926) as supported by its priority document, Provisional Application 60/363366 ("Ochoa"), in view of Jeffrey (Am. J. Respir. Crit. Care Med. (2001) Vol. 164: pp. S28-S38) ("Jeffrey").

Claims 21-24 have been cancelled, rendering this rejection moot against those claims.

Claims 1, 4, 6, 12 and 13, as amended, are drawn to a method of administering an agent to a mammal which has airway subepithelial fibrosis and matrix deposition, in which the agent

inhibits a component of an arginine metabolic pathway and is not in a nitric oxide synthase (NOS).

The Office cited Ochoa as allegedly teaching "administering lysine which inhibits a cationic amino acid transporter 2 for treating chronic obstructive pulmonary disease," (office action, p. 4 lines 9-12.) Jeffrey is cited by the Office as allegedly teaching "that … COPD [is] accompanied with structural changes known as chronic airway remodeling," (office action, p. 5, lines 2-3.) The Office contends that "one of ordinary skill in the art seeking to treat chronic obstructive pulmonary disease, in the presence or absence of chronic airway remodeling, would have been motivated to use the agents taught by Ochoa et al.," (office action, p. 5, lines 13-15.)

The Applicants respectfully traverse this rejection. Claims 1, 4, 6, 12 and 13, as amended, provide the treating of airway subepithelial fibrosis and matrix deposition. Jeffrey teaches that subepithelial fibrosis and matrix deposition cause thickening of the reticular basement membrane ("RBM") (Jeffery at p. S32, column 1, entire first full paragraph), but that "RBM thickness in smokers with COPD was within the normal range," (Jeffrey, p. S31, column 1, lines 18-19). Jeffrey thus teaches that structural changes associated with COPD do not encompass subepithelial fibrosis and matrix deposition, and therefore the skilled artisan would not be motivated to employ Ochoa's treatment for COPD to treat airway subeptithelial fibrosis and matrix deposition, as provided in the claims.

Furthermore, the combination of Jeffrey and Ochoa fail to teach each and every element of the claims (MPEP 2141 part I). Applicants request that the rejection of claims 1, 4, 6, 12 and 13 under 35 USC 103(a) for allegedly being unpatentable over Ochoa be withdrawn.

Claims 1, 4, 6, 8, 12 and 13

Claims 1, 4, 6, 8, 12 and 13 stand rejected under 35 USC 103(a) for allegedly being unpatentable over Rothenberg *et al.* (US 2003/0166562) ("Rothenberg"), in view of Jeffrey (Am. J. Respir. Crit. Care Med. (2001) Vol. 164: pp. S28-S38) ("Jeffrey").

Rothenberg is cited by the Office as allegedly teaching "administering a therapeutically effective amount of an agent to a mammal with asthma which inhibits CAT2 …," (office action, p. 6, lines 11-13.) Jeffery is cited by the Office as allegedly teaching "that asthma and COPD are accompanied by structural changes known as chronic airway remodeling," (office action, p. 5, lines 2-3.) The Office contends that "it would have been to one of ordinary skill in the art that

a method of providing an agent to a mammal with asthma would also be providing an agent to a mammal with chronic airway remodeling," (office action, last line p. 6 – p. 7, lines 1-2.)

Applicants respectfully traverse. As the Office points out, "Rothenberg *et al.* did not explicitly anticipate administering an agent to a mammal that has chronic airway remodeling," (office action, p. 7, lines 6-7.) Furthermore, Rothenberg fails to provide any teaching or motivation for treating airway subepithelial fibrosis and matrix deposition, but simply describes the expression of arginase 1 in tissues that are not expected by the skilled artisan to be involved in airway subepithelial fibrosis and matrix deposition. Rothenberg teaches the expression of arginase 1 in those tissues showing inflammation after OVA challenge, such as for example in the perivascular regions (Rothenberg, paragraph [0067]. Rothenberg does not teach expression of arginase 1 in airway subepithelium and/or matrix.

Applicants submit that the skilled artisan would have no reason to expect, based upon the vascular and blood cell inflammation expression data provided in Rothenberg (*e.g.,* paragraph [0067]), that administration of an agent that can affect the arginase pathway would have an effect on subepithelial fibrosis and matrix deposition. Furthermore, Jeffrey teaches that "[i]t is equally plausible that the processes responsible for the development of chronic inflammation are distinct from those responsible for remodeling," and "those agents that are effective anti-inflammatory compounds will not necessarily prevent or attenuate the process of remodeling" (Jeffrey, p. S28, column 2, second paragraph, line 11 through p. S29, column 1, lines 2 and 4-6.) Thus, Jeffrey teaches that one skilled in the art can not predict success in combining the alleged anti-inflammatory agent of Rothenberg to the treatment of subepithelial fibrosis and matrix remodeling.

Applicants contend that the Office has not sufficiently established a *prima facie* case of obviousness, as required. The MPEP at 2141, part I states, "When considering obviousness of a combination of known elements, the operative question is thus 'whether the improvement is more than the predictable use of prior art elements according to their established functions.' *KSR International Co. v. Teleflex Inc. (KSR)* at ___, 82 USPQ2d at 1396." Applicants submit that one of ordinary skill in the art could not have predicted, based on Jeffrey's "equal plausibility" (*i.e.,* 50/50 chance) hypothesis, that administering an agent allegedly taught to be involved in an inflammation process would have an effect on airway remodeling.

Therefore, Applicants submit that claims 1, 4, 6, 12 and 13 are not obvious under 37 CFR 103(a) over Rothenberg in view of Jeffrey. Applicants request that the rejection be withdrawn.

Claim 10

Claim 10 stands rejected under 35 USC 103(a) for allegedly being unpatentable over Rothenberg *et al.* (US 2003/0166562) ("Rothenberg"), in view of Jeffrey (Am. J. Respir. Crit. Care Med. (2001) Vol. 164: pp. S28-S38) ("Jeffrey") and in further view of Hannon (Nature (2002) Vol. 418: pp. 244-251) ("Hannon".)

Rothenberg and Jeffery are cited by the Office against claims 1 and 8, which are antecedent to claim 10, as described above. Hannon is cited by the Office for allegedly teaching "that siRNA may be synthesized to target and silence genes of interest ...," (office action, p. 8, lines 1-2.)

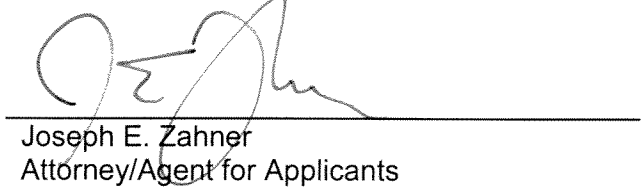
Claim 10 provides a method of treating chronic airway remodeling by administering a siRNA that inhibits CAT2 expression.

As argued in the preceding section, Applicants traversed the rejection of claims 1, 4, 6, 8, 12 and 13 under 35 USC 103(a) for allegedly being unpatentable over Rothenberg, in view of Jeffrey. Claim 10 depends from claim 8, which depends from claim 1. Regarding claim 10, Hannon fails to cure the defects of Rothenberg in view of Jeffrey.

Therefore, Applicants submit that claim 10 is not obvious under 37 CFR 103(a) over Rothenberg in view of Jeffrey further in view of Hannon. Applicants request that the rejection be withdrawn.

CONCLUSION

Based on the foregoing, it is respectfully submitted that claims 1, 4, 6, 8, 10, 12, and 13 are allowable over the art of record. A timely notice of allowance is respectfully requested.



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